Transcript Details
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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Reassessing the Full Clinical Picture of ADHD

Dr. Turck:
And how do these associated features impact caregivers?

Dr. Childress:
All of these can really take a toll on family and caregivers. They're usually the ones managing social interactions – or avoiding them altogether. They're also coordinating healthcare and advocating for the right educational support.[26,27] That kind of pressure can cause emotional distress and put a strain on family and work life.[26,28]

Dr. Turck:
That makes sense. So, could you tell us a bit about the comorbidities associated with ADHD?

Dr. Childress:
Of course. One of the more complex aspects of ADHD is that it often doesn't exist in isolation. In fact up to 50 percent of people with ADHD also experience comorbid psychiatric conditions, such as anxiety.[6,29-31] And when those conditions show up alongside ADHD, it can make everything more complicated.

For example, people who have both ADHD and anxiety often have a harder time at work, may have a more severe clinical picture, and tend to report a lower overall quality of life.[32,33] In fact, there are higher rates of hospitalization, suicidal behaviors, and susceptibility for anger.[32]

And because the symptom profiles overlap and the impact on quality of life is similar, it can be easy to misdiagnose or miss a co-occurring condition entirely.[34] Sometimes the ADHD gets diagnosed, but the anxiety doesn't. Or the reverse happens. And if you're only treating part of what's going on, it can delay real progress or lead to the wrong kind of treatment altogether.[34]

I saw a 27-year-old with ADHD who had a lot of physical symptoms indicative of anxiety – sexual dysfunction, back pain, tension headaches, irritable bowel syndrome. Although he wasn't complaining about anxiety, when we queried he met criteria for generalized anxiety disorder. So, it's important to ask about anxiety because ADHD patients present with a lot of physical symptoms, too.

Dr. Turck:
So, coming back to how we opened this conversation, and given the heterogeneity of ADHD, how should clinicians adapt their assessment approach to avoid diagnostic complications and capture the full spectrum of presentation?

Dr. Childress:
Right, as I mentioned before, ADHD isn't a one-size-fits-all condition, and that's exactly what makes it so challenging to diagnose and manage, it's heterogeneous, so it looks different from person to person.[3,4] And because of this variability, clinicians really need to move beyond a checklist approach that focuses only on attention and hyperactivity.

During my work on clinical trials, I assess patients more thoroughly. But I don't think most clinicians understand the associated features well and don't have time to assess all of them. Instead, assessment should be more comprehensive, looking at emotional and executive function difficulties,[1] common comorbidities like anxiety,[34] and the ways symptoms are impacting real-world functioning, in work, school, relationships, and daily life.[7,9,19-21,32]

This broader approach not only helps capture the full clinical presentation of ADHD, but also leads to more effective, individualized

treatment plans. After all, what works for one person with ADHD may not work at all for someone else.

ReachMD Announcer:
Chapter 2: Unpacking the Neurobiology of ADHD

Dr. Turck:
Let's shift gears now and consider the complexity of ADHD through a neurobiological lens. Do you think it's time we expand our understanding of neurotransmitters and the pathways involved in ADHD's underlying biology?

Dr. Childress:
Yes, when we talk about ADHD, dopamine and norepinephrine usually get most of the spotlight, and that makes sense. Dopamine is tied to movement, mood disorders, attention, learning and memory, and reward processing.[35] Norepinephrine also helps with attention, as well as arousal signal-to-noise processing, mood regulation, and stress response.[35] These are the core symptoms of ADHD, so it makes sense that these neurotransmitters have been a big focus in both research and treatment when developing stimulants that target those systems.[36]

But what's often missing from the conversation is serotonin, it's a big piece of the puzzle that's starting to get more attention.[36,37] Serotonin affects things like mood, perception, appetite, aggression, anxiety, and reward processing, all of which can be disrupted or show up as common comorbidities in people with ADHD.[37] And since we know that ADHD isn't just about focus or hyperactivity but also emotional dysregulation and executive dysfunction, it makes sense that serotonin might be apart of the picture too.[1] Growing evidence suggests that dysregulation of serotonin signaling, particularly in the prefrontal cortex and amygdala, may contribute to ADHD by affecting impulse control, mood regulation, and emotional stability.[37,38] We also know that serotonergic neurons innervate much of the central nervous system, including the prefrontal cortex and striatum, both of which are key areas involved in the neurobiology of ADHD.[39]

Dr. Turck:
So, Dr. Childress, given that context, how does the interplay between neurotransmitters help explain the wide variability in how ADHD presents from one person to another?

Dr. Childress:
A big part of that variability may come down to the interplay between dopamine, norepinephrine, and serotonin. No two people with ADHD have exactly the same neurochemical profile. One person might have more issues tied to dopamine, while another might have serotonin-related challenges like mood instability or anxiety.[36,40]

On the flip side, it's also important to understand that these neurotransmitter systems are interconnected, so an imbalance in one can affect the others. This also helps explain the wide range of ADHD presentations, from a hyperactive child to an adult dealing with more focus and emotional regulation.[35,36] And that's exactly why we need to consider this neurobiological complexity into both clinical assessment and treatment.

ReachMD Announcer:
Chapter 3: Rethinking the Approach to ADHD Treatment

Dr. Turck:
Now, Dr. Childress, there are currently a few medications on the market that treat ADHD, but how effective are they in addressing the broader challenges patients face in daily life?

Dr. Childress:
Well, many of the stimulants on the market have been shown to be effective at addressing the core ADHD symptoms, like inattention and hyperactivity, by targeting dopaminergic and noradrenergic pathways.[35,36] But less than 30 percent of individuals report they are fully satisfied with their current stimulant therapy.[41] And retrospective claims analyses using IBM MarketScan data from 2014 to 2018 looked at nearly 80,000 children and adolescents and around 123,000 adults with ADHD. In each study, over 90 percent of these patients started out on stimulants.[42,43] For Children, within the first year, 59 percent had a change in their treatment, and about 21 percent stopped their medication altogether.[43]

When the researchers focused just on adolescents, the numbers were even higher. About two-thirds had some kind of treatment change within 12 months, and third discontinued medication, and strikingly, 33.5 percent of those who stopped did so within the very first month.[43] In adults too, about 50.2 percent of patients had a treatment change in seven months. 22.5 percent of patients discontinued,

and nearly 45 percent of those who discontinued did so in the first month.[42]

Dr. Turck:
Well that's interesting. What might be contributing to these persistent symptoms and treatment dissatisfaction?

Dr. Childress:
One reason for this may be that we're not addressing the full neurochemical landscape of ADHD. And that may contribute to why so many people, even on treatment, continue to experience residual symptoms of emotional dysregulation and executive dysfunction.[1,11,44,45] What's more, nearly half of patients continue to struggle with emotional dysregulation, and over a third report ongoing executive function deficits, like problems with organization, planning, and follow-through, while taking medication.[11,18,49] So we might be missing the broader neurochemical picture.

Another big challenge is side effects. 95 percent of adults on ADHD medications in the U.S. report experiencing at least one ongoing symptom or treatment-related adverse effect. These can include sleep issues and mood swings.[11] And individuals with comorbidities such as anxiety may show lack of improvement or even worsening anxiety symptoms while treating their ADHD.[11,41,49,50] These treatment side effects negatively affect quality of life and can also contribute to poor adherence.[41,49]Actually, two thirds of patients end up switching treatments within a year, which points to a lack of sustained satisfaction or effectiveness.[11,51,52]

Dr. Turck:
So with that in mind, what would an integrative, neurobiologically aligned treatment approach for ADHD look like in clinical practice?

Dr. Childress:
Providers should look beyond just targeting the core symptoms of inattention, hyperactivity, and impulsivity and take into account the full spectrum of the disorder.[40] So making sure to consider all three neurotransmitter systems—dopamine, norepinephrine, and serotonin—to better address core and associated symptoms,[40] actively screen for and treat comorbid psychiatric conditions like anxiety,[34] and use a personalized approach, since the neurobiological profile and symptom presentation can vary from one individual to another.[3,4] And I believe asking about associated features at the initial visit and following those symptoms at subsequent visits is important. We need to identify comorbid symptoms and make sure we assess changes at follow-up visits to ensure that we're making treatment adjustments.

Dr. Turck:
With those final thoughts in mind, I want to thank Dr. Ann Childress, for helping us better understand the neurobiology and treatment of ADHD.

Dr. Childress, it was great speaking with you today.

Dr. Childress:
Thank you!

Dr. Turck:
For ReachMD, I'm Dr. Charles Turck.

ReachMD Announcer:
This medical industry feature was sponsored by Otsuka. If you missed any part of this discussion, visit Industry Features on ReachMD.com, where you can Be Part of the Knowledge.

References:

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. American Psychiatric Association Publishing; 2022.
2. Sibley MH, Swanson JM, Arnold LE, et al. Defining ADHD symptom persistence in adulthood: optimizing sensitivity and specificity. *J Child Psychol Psychiatry*. Jun 2017;58(6):655–662. doi:10.1111/jcpp.12620
3. Lapalme M, Déry M, Lemieuxet A. Developmental course of ADHD symptoms based on multirater report in girls and boys with or without a disruptive behavior disorder. *J Emot Behav Disord*. 2018;26(2):106–118. doi:10.1177/1063426617712500
4. Øie M, Hovik KT, Andersen PN, Czajkowski NO, Skogli EW. Gender differences in the relationship between changes in ADHD symptoms, executive functions, and self- and parent-report depression symptoms in boys and girls with ADHD: a 2-year follow-up study. *J Atten Disord*. Mar 2018;22(5):446–459. doi:10.1177/1087054716664407
5. Staley BS, Robinson LR, Claussen AH, et al. Attention-deficit/hyperactivity disorder diagnosis, treatment, and telehealth use in adults - National Center for Health Statistics Rapid Surveys System, United States, October-November 2023. *MMWR Morb*

Mortal Wkly Rep. Oct 10 2024;73(40):890–895. doi:10.15585/mmwr.mm7340a1
6. Danielson ML, Claussen AH, Bitsko RH, et al. ADHD prevalence among U.S. children and adolescents in 2022: diagnosis, severity, co-occurring disorders, and treatment. *J Clin Child Adolesc Psychol*. May–Jun 2024;53(3):343–360. doi:10.1080/15374416.2024.2335625
7. Soler-Gutierrez AM, Perez-Gonzalez JC, Mayas J. Evidence of emotion dysregulation as a core symptom of adult ADHD: A systematic review. *PLoS One*. 2023;18(1):e0280131. doi:10.1371/journal.pone.0280131
8. Bodalski EA, Flory K, Meinzer MC. A scoping review of factors associated with emotional dysregulation in adults with ADHD. *J Atten Disord*. Nov 2023;27(13):1540–1558. doi:10.1177/10870547231187148
9. Shaw P, Stringaris A, Nigg J, Leibenluft E. Emotion dysregulation in attention deficit hyperactivity disorder. *Am J Psychiatry*. Mar 2014;171(3):276–93. doi:10.1176/appi.ajp.2013.13070966
10. Perugi G, Pallucchini A, Rizzato S, Pinzone V, De Rossi P. Current and emerging pharmacotherapy for the treatment of adult attention deficit hyperactivity disorder (ADHD). *Expert Opin Pharmacother*. Aug 2019;20(12):1457–1470. doi:10.1080/14656566.2019.1618270
11. Schein J, Cloutier M, Gauthier-Loiselle M, Bungay R, Guerin A, Childress A. Symptoms associated with ADHD/treatment-related adverse side effects and their impact on quality of life and work productivity in adults with ADHD. *Curr Med Res Opin*. Jan 2023;39(1):149–159. doi:10.1080/03007995.2022.2122228
12. van Stralen J. Emotional dysregulation in children with attention-deficit/hyperactivity disorder. *Atten Defic Hyperact Disord*. Dec 2016;8(4):175–187. doi:10.1007/s12402-016-0199-0
13. Willcutt EG, Doyle AE, Nigg JT, Faraone SV, Pennington BF. Validity of the executive function theory of attention-deficit/hyperactivity disorder: a meta-analytic review. *Biol Psychiatry*. Jun 1 2005;57(11):1336–46. doi:10.1016/j.biopsych.2005.02.006
14. Silverstein MJ, Faraone SV, Leon TL, Biederman J, Spencer TJ, Adler LA. The relationship between executive function deficits and DSM-5-defined ADHD symptoms. *J Atten Disord*. Jan 2020;24(1):41–51. doi:10.1177/1087054718804347
15. Kofler MJ, Irwin LN, Soto EF, Groves NB, Harmon SL, Sarver DE. Executive Functioning Heterogeneity in Pediatric ADHD. *J Abnorm Child Psychol*. Feb 2019;47(2):273–286. doi:10.1007/s10802-018-0438-2
16. Adler LA, Faraone SV, Spencer TJ, Berglund P, Alperin S, Kessler RC. The structure of adult ADHD. *Int J Methods Psychiatr Res*. Mar 2017;26(1)doi:10.1002/mpr.1555
17. Kosheleff AR, Mason O, Jain R, Koch J, Rubin J. Functional impairments associated with ADHD in adulthood and the impact of pharmacological treatment. *J Atten Disord*. May 2023;27(7):669–697. doi:10.1177/10870547231158572
18. Brown TE, Brams M, Gao J, Gasior M, Childress A. Open-label administration of lisdexamfetamine dimesylate improves executive function impairments and symptoms of attention-deficit/hyperactivity disorder in adults. *Postgrad Med*. Sep 2010;122(5):7–17. doi:10.3810/pgm.2010.09.2196
19. Arnold LE, Hodgkins P, Kahle J, Madhoo M, Kewley G. Long-term outcomes of ADHD: academic achievement and performance. *J Atten Disord*. Jan 2020;24(1):73–85. doi:10.1177/1087054714566076
20. Holst Y, Thorell LB. Functional impairments among adults with ADHD: a comparison with adults with other psychiatric disorders and links to executive deficits. *Appl Neuropsychol Adult*. May–Jun 2020;27(3):243–255. doi:10.1080/23279095.2018.1532429
21. Rinsky JR, Hinshaw SP. Linkages between childhood executive functioning and adolescent social functioning and psychopathology in girls with ADHD. *Child Neuropsychol*. 2011;17(4):368–90. doi:10.1080/09297049.2010.544649
22. Aduen PA, Kofler MJ, Sarver DE, Wells EL, Soto EF, Cox DJ. ADHD, depression, and motor vehicle crashes: A prospective cohort study of continuously-monitored, real-world driving. *J Psychiatr Res*. Jun 2018;101:42–49. doi:10.1016/j.jpsychires.2018.02.026
23. French B, Nalbant G, Wright H, et al. The impacts associated with having ADHD: an umbrella review. *Front Psychiatry*. 2024;15:1343314. doi:10.3389/fpsyt.2024.1343314
24. Balazs J, Kereszteny A. Attention-deficit/hyperactivity disorder and suicide: a systematic review. *World J Psychiatry*. Mar 22 2017;7(1):44–59. doi:10.5498/wjp.v7.i1.44
25. Van Eck K, Ballard E, Hart S, Newcomer A, Musci R, Flory K. ADHD and suicidal ideation: the roles of emotion regulation and depressive symptoms among college students. *J Atten Disord*. Aug 2015;19(8):703–14. doi:10.1177/1087054713518238
26. Fridman M, Banaschewski T, Sikirica V, Quintero J, Erder MH, Chen KS. Factors associated with caregiver burden among pharmacotherapy-treated children/adolescents with ADHD in the Caregiver Perspective on Pediatric ADHD survey in Europe. *Neuropsychiatr Dis Treat*. 2017;13:373–386. doi:10.2147/NDT.S121391
27. McKenna K, Wanni Arachchige Dona S, Gold L, Dew A, Le HND. Barriers and enablers of service access and utilization for children and adolescents with attention deficit hyperactivity disorder: a systematic review. *J Atten Disord*. Feb 2024;28(3):259–278. doi:10.1177/10870547231214002

28. Chen Q, Larsson H, Almqvist C, et al. Association between pharmacotherapy for ADHD in offspring and depression-related specialty care visits by parents with a history of depression. *BMC Psychiatry*. Jul 17 2019;19(1):224. doi:10.1186/s12888-019-2211-7
29. Choi WS, Woo YS, Wang SM, Lim HK, Bahk WM. The prevalence of psychiatric comorbidities in adult ADHD compared with non-ADHD populations: a systematic literature review. *PLoS One*. 2022;17(11):e0277175. doi:10.1371/journal.pone.0277175
30. Leon-Barriera R, Ortegon RS, Chaplin MM, Modesto-Lowe V. Treating ADHD and comorbid anxiety in children: a guide for clinical practice. *Clin Pediatr (Phila)*. Jan 2023;62(1):39–46. doi:10.1177/00099228221111246
31. Babinski DE, Neely KA, Ba DM, Liu G. Depression and suicidal behavior in young adult men and women with ADHD: evidence from claims data. *J Clin Psychiatry*. Sep 22 2020;81(6)doi:10.4088/JCP.19m13130
32. Quenneville AF, Kalogeropoulou E, Nicastro R, Weibel S, Chanut F, Perroud N. Anxiety disorders in adult ADHD: a frequent comorbidity and a risk factor for externalizing problems. *Psychiatry Res*. Apr 2022;310:114423. doi:10.1016/j.psychres.2022.114423
33. Katzman MA, Bilkey TS, Chokka PR, Fallu A, Klassen LJ. Adult ADHD and comorbid disorders: clinical implications of a dimensional approach. *BMC Psychiatry*. Aug 22 2017;17(1):302. doi:10.1186/s12888-017-1463-3
34. Jain R, Jain S, Montano CB. Addressing Diagnosis and Treatment Gaps in Adults With Attention-Deficit/Hyperactivity Disorder. *Prim Care Companion CNS Disord*. Sep 7 2017;19(5)doi:10.4088/PCC.17nr02153
35. da Silva BS, Grevet EH, Silva LCF, Ramos JKN, Rovaris DL, Bau CHD. An overview on neurobiology and therapeutics of attention-deficit/hyperactivity disorder. *Discov Ment Health*. Jan 5 2023;3(1):2. doi:10.1007/s44192-022-00030-1
36. Koirala S, Grimsrud G, Mooney MA, et al. Neurobiology of attention-deficit hyperactivity disorder: historical challenges and emerging frontiers. *Nat Rev Neurosci*. Dec 2024;25(12):759–775. doi:10.1038/s41583-024-00869-z
37. Pourhamzeh M, Moravej FG, Arabi M, et al. The roles of serotonin in neuropsychiatric disorders. *Cell Mol Neurobiol*. Aug 2022;42(6):1671–1692. doi:10.1007/s10571-021-01064-9
38. Faraone SV, Bellgrove MA, Brikell I, et al. Attention-deficit/hyperactivity disorder. *Nat Rev Dis Primers*. Feb 22 2024;10(1):11. doi:10.1038/s41572-024-00495-0
39. Conio B, Martino M, Magioncalda P, et al. Opposite effects of dopamine and serotonin on resting-state networks: review and implications for psychiatric disorders. *Mol Psychiatry*. Jan 2020;25(1):82–93. doi:10.1038/s41380-019-0406-4
40. Wang Y, Wang T, Du Y, et al. Polygenic risk of genes involved in the catecholamine and serotonin pathways for ADHD in children. *Neurosci Lett*. Aug 24 2021;760:136086. doi:10.1016/j.neulet.2021.136086
41. National Academies of Sciences, Engineering, and Medicine. 2024. *Adult Attention-Deficit/Hyperactivity Disorder: Diagnosis, Treatment, and Implications for Drug Development: Proceedings of a Workshop*. Washington, DC: The National Academies Press. doi:10.17226/27770.
42. Schein J, Childress A, Adams J, et al. Treatment patterns among adults with attention-deficit/hyperactivity disorder in the United States: a retrospective claims study. *Curr Med Res Opin*. Nov 2021;37(11):2007–2014. doi:10.1080/03007995.2021.1968814
43. Schein J, Childress A, Adams J, et al. Treatment patterns among children and adolescents with attention-deficit/hyperactivity disorder in the United States - a retrospective claims analysis. *BMC Psychiatry*. Aug 18 2022;22(1):555. doi:10.1186/s12888-022-04188-4
44. Stahl SM. *Stahl's essential psychopharmacology : neuroscientific basis and practical applications*. Fifth edition. ed. Cambridge University Press; 2021:pages cm.
45. Faraone SV, Radonjić NV. Neurobiology of Attention Deficit Hyperactivity Disorder. In: Tasman A, Riba MB, Alarcón RD, et al, eds. *Tasman's Psychiatry*. Springer International Publishing; 2020:1–28.
46. Moukhtarian TR, Cooper RE, Vassos E, Moran P, Asherson P. Effects of stimulants and atomoxetine on emotional lability in adults: a systematic review and meta-analysis. *Eur Psychiatry*. Jul 2017;44:198–207. doi:10.1016/j.eurpsy.2017.05.021
47. Lenzi F, Cortese S, Harris J, Masi G. Pharmacotherapy of emotional dysregulation in adults with ADHD: a systematic review and meta-analysis. *Neurosci Biobehav Rev*. Jan 2018;84:359–367. doi:10.1016/j.neubiorev.2017.08.010
48. Isfandnia F, El Masri S, Radua J, Rubia K. The effects of chronic administration of stimulant and non-stimulant medications on executive functions in ADHD: A systematic review and meta-analysis. *Neurosci Biobehav Rev*. Jul 2024;162:105703. doi:10.1016/j.neubiorev.2024.105703
49. Brown TE, Romero B, Sarocco P, Atkins N, Schwartz EJ, Rhoten S. The patient perspective: unmet treatment needs in adults with attention-deficit/hyperactivity disorder. *Prim Care Companion CNS Disord*. Jun 6 2019;21(3)doi:10.4088/PCC.18m02397
50. Schein J, Cloutier M, Bungay R, Gauthier-Loiselle M, Childress A. Costs associated with adverse events during treatment episodes for adult attention-deficit/hyperactivity disorder. *J Med Econ*. Jan–Dec 2024;27(1):653–662. doi:10.1080/13696998.2024.2342749
51. Schein J, Childress A, Gagnon-Sanschagrin P, et al. Treatment patterns among patients with attention-deficit/hyperactivity

disorder and comorbid anxiety and/or depression in the United States: a retrospective claims analysis. *Adv Ther*. May 2023;40(5):2265–2281. doi:10.1007/s12325-023-02458-5

52. Schein J, Cloutier M, Gauthier-Loiselle M, et al. Quality of life and outcomes associated with adverse effects in pediatric patients with attention-deficit/hyperactivity disorder and their parents/caregivers. *J Child Adolesc Psychopharmacol*. Feb 2025;35(1):49–60. doi:10.1089/cap.2024.0061
53. Frank E, Ozon C, Nair V, Othee K. Examining why patients with attention-deficit/hyperactivity disorder lack adherence to medication over the long term: a review and analysis. *J Clin Psychiatry*. Nov 2015;76(11):e1459–68. doi:10.4088/JCP.14r09478